Reviewer: ORNL **Date:** February 26, 2008
Risk Manager (EPA): 25

STUDY TYPE: Acute Inhalation Toxicity – Rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: Paradox (Paraquat dichloride, 5.00%; Lot No. 040607; dark green liquid, pH 4.9, soluble in methanol, ethanol, acetone, corn oil, and mineral oil)

CITATION: Durando, J. (2007) Paradox – Acute Inhalation Toxicity Study in Rats. Study Number 21927. Eurofins/Product Safety Laboratories, 2394 US Highway 130, Dayton, NJ 08810. September 25, 2007. MRID 47257203.

SPONSOR: EDM Industries, Inc., P.O. Box 8552, Porterville, CA 93258

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 47257203), fifteen male and fifteen female young adult Sprague-Dawley rats (age: 9-10 weeks; body weight: males: 307-356 g and females: 194-264 g; source: Ace Animals, Inc., Boyertown, PA) were exposed by nose-only inhalation to Paradox (Paraquat dichloride, 5.00%; Lot No. 040607) for 4 hours and 1 minute at concentrations of 0.053, 0.53, or 2.02 mg/L. The animals were observed for 14 days. The MMADs for exposure level 0.053 mg/L were 1.8 and 1.7 μm and the GSD 2.60 and 2.57 at 1.5 and 3 hours, respectively; for exposure level 0.53 mg/L were 1.9 and 2.1 μm and the GSD 1.90 and 1.89 at 1.5 and 3 hours, respectively; and for exposure level 2.02 mg/L were 2.3 and 2.2 μm and the GSD 2.07 and 1.83 at 1.5 and 3 hours, respectively.

All 0.053 mg/L animals survived the study and all animals exposed to 0.53 or 2.02 mg/L died on day of exposure or days 1-3 or were euthanized on days 3 or 6. Prior to death, dyspnea, moist rales, hunched posture, hypoactivity, red nasal discharge, irregular respiration, reduced fecal volume, facial staining, and/or prone posture were noted from the decedents. One male and one female exposed to 0.053 mg/L were hypoactive upon removal from the chamber through one hour post exposure, and along with the other survivors appeared active and healthy till the end of the study. All 0.053 mg/L animals gained weight throughout the study. Dark mottled/red/extremely red/edematous/fluid filled lungs, rigor mortis appearance, discolored liver, moderately red/slightly yellow intestines, and/or empty stomachs were noted from the decedents. No gross abnormalities were noted in any 0.053 mg/L animal at necropsy.

LC_{50} Males > 0.053 mg/L and < 0.53 mg/L
LC_{50} Females > 0.053 mg/L and < 0.53 mg/L
LC_{50} Combined > 0.053 mg/L and < 0.53 mg/L

PARADOX is in EPA Toxicity Category II.

This study is classified as acceptable. It does satisfy the guideline requirements for an acute inhalation study (OPPTS 870.1300; OECD 403) in the rat.

COMPLIANCE: Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Nominal Conc. (mg/L)	Gravimetric Conc. (mg/L)	MMAD µm	GSD	Mortality/Number Tested		
				Males	Females	Combined
1.02	0.053	1.8, 1.7	2.60, 2.57	0/5	0/5	0/10
8.38	0.53	1.9, 2.1	1.90, 1.89	5/5	5/5	10/10
26.75	2.02	2.3, 2.2	2.07, 1.83	5/5	5/5	10/10

Test Atmosphere / Chamber Description: The exposure atmosphere was generated using a 1/4 inch JCO atomizer (Spraying Systems Co.), FC3 fluid cap, and AC1502 air cap (both caps Robert Miller Associates). The test material was metered to the atomization nozzle through Tygon tubing using a pump. Filtered air was supplied by an air compressor connected to the spray atomization nozzle. Additional compressed mixing air was supplied from a compressed air tank. Animals were individually housed in polycarbonate holding tubes sealed to the chamber during exposure. The exposure chamber was a Mini Nose-Only Chamber (ADG Developments Ltd.).

Gravimetric Conc. (mg/L):	**0.053**	**0.53**	**2.02**
Chamber Volume (L):	**6.7**	**6.7**	**6.7**
Total Airflow (L/min):	**25.7**	**25.4**	**25.3**
Temperature	**22-23°C**	**24°C**	**20-22°C**
Relative Humidity	**66-69%**	**60-65%**	**53-57%**
Time to equilibrium:	**1.2 minute**	**1.2 minute**	**1.2 minute**

Test atmosphere concentration: During exposure, gravimetric samples were collected five or six times from the breathing zone of the animals, using glass fiber filters. Filter papers were weighed before and after collection to determine the mass collected. The value was divided by the total volume of air sampled to determine the chamber concentration.

Particle size determination: Particle size for each exposure concentration was determined twice using an eight-stage Andersen cascade impactor. The test material concentration collected at each stage was determined gravimetrically. The mass median aerodynamic diameter and geometric standard deviation were determined graphically using two-cycle logarithmic probit axes.

A. **Mortality:** All 0.053 mg/L animals survived the study and all animals exposed to 0.53 or 2.02 mg/L died on the day of exposure or days 1-3 or were euthanized on days 3 or 6.

B. **Clinical observations:** Prior to death, dyspnea, moist rales, hunched posture, hypoactivity, red nasal discharge, irregular respiration, reduced fecal volume, facial staining, and/or prone posture were noted from the decedents. One male and one female exposed to 0.053 mg/L were hypoactive upon removal from the chamber through one hour post exposure, and along with the other survivors appeared active and healthy till the end of the study. All 0.053 mg/L animals gained weight throughout the study.

C. **Gross necropsy:** Dark mottled/red/extremely red/edematous/fluid filled lungs, rigor mortis appearance, discolored liver, moderately red/slightly yellow intestines, and/or empty stomachs were noted from the decedents. No gross abnormalities were noted in any 0.053 mg/L animal at necropsy.

D. **Reviewer's conclusions:** This reviewer agrees with the study author regarding the acute inhalation LC_{50} and suggests the male and female combined LC_{50} should be > 0.053 mg/L and < 0.53 mg/L.